

Claims

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1. A process for measuring enzyme activities in liquids, which comprises withdrawing enzyme inhibitors, that correspond to at least one of the enzymes in the sample, adding a substrate to the sample manipulated in this manner, so as to get cleavage products from the substrate by reacting with the enzyme, and detecting the increasing concentration per unit of time of at least one of this cleavage products during an incubation time.

The said process is characterized by withdrawing the enzyme inhibitors from the sample by means of chromatography.

2. A process according to claim 1 characterized in that the sample passes through a column (1) filled with a chromatographic carrier, that is treated with a substance capable of binding the enzyme inhibitors.

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3. A process according to one of the claims 1 or 2 characterized in that the said sample is diluted with a column buffer.

4. A process according to one of the claims 1 to 3 characterized in that a suitable measuring buffer is added to the said sample in order to produce definite experimental conditions.

5. A process according to one of the claims 1 to 4 characterized in that the substrate is thermostated at least during the incubation time.

6. A process according to one of the claims 1 to 5 characterized in that the increasing concentration of one of the cleavage products of the substrate is detected by means of fluorescence measurements.

7. A device for measuring the activity of enzymes in liquids by means of a process according to one the claims 1 to 6 and 23 to 27, in particular characterized in that there is provided a column (1) filled with a chromatographic carrier treated with a substance capable of binding such enzyme inhibitors which correspond to at least one enzyme in

the sample, and that there is a valve/pump arrangement (7, 11, 14, 15) connected in series to the end of the column (1), so as to fill at least one test vessel with a substrate and at least a part of the sample, and that there is provided a detector for measuring the increase of the concentration per unit of time of at least one cleavage product.

8. A device according to claim 7 characterized in that the column (1) can be used repeatedly, as there is an excess of the substance corresponding to the capacity of the column (1).

9. A device according to one of the claims 7 or 8 characterized in that the column (1) is exchangeable.

10. A device according to one of the claims 7 to 9 characterized in that the sample supply tube (2) is alternatively fed out of the sample supply (3) or a reservoir (4) containing column buffer.

11. A device according to claim 10 characterized in that there is provided a control device (8) connected in series to the column (1) in order to check the purity of the column buffer discharged from the column (1).

12. A device according to claim 11 characterized in that the said control device (8) works photometrically.

13. A device according to claim 11 characterized in that the said control device is also able to measure the electrolytic conductance of liquids.

14. A device according to one of the claims 10 to 13 characterized in that there is an arrangement (9) connected in series to the column (1) for measuring the degree of dilution of the discharged sample caused by the column buffer.

15. A device according to claim 14 characterized in that the said arrangement (9) is able to measure the volume of liquids.

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16. A device according to one of the claims 10 to 15 characterized in that there is a device for mixing (10) connected in series to the column (1) as to produce a homogenous mixture of the said sample with the column buffer.

17. A device according to one of the claims 7 to 16 characterized in that it enables one by means of the valve/pump arrangement (11, 14, 15) to admix a measuring buffer to the said sample, and if need be, to the column buffer and to the substrate in the test tube (5) so as to produce definite experimental conditions.

18. A device according to one of the claims 7 to 17 characterized in that the detector is including a device for measuring fluorescence.

19. A device according to one of the claims 7 to 18 characterized in that there are provided means to thermostate the test tube (5).

20. A device according to one of the claims 7 to 19 characterized in that there is at least one switching valve (6) between the sample supply tube (2) and the column (1) which enables the sample alternatively to pass through the column or bypass the column in order to get into the test tube (5).

21. A device according to one of the claims 7 to 20 characterized in that at least one valve (16) is provided in order to pass a buffer as a wash liquid at least through the column (1) and the valve/pump arrangement.

22. A device according to one of the claims 7 to 21 characterized in that there is provided a computer (18) in order to run and control the sample feeding and if need be, the column buffer feeding, if need be, the degree of dilution of the sample to be measured, and if need be, the mixing, charging of the test tubes (5) and the detection and evaluation of the concentration increase per unit of time of at least one of the cleavage products of the substrate.

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23. A process for measuring enzyme inhibitors in liquids especially according to the claims 1 to 6, which comprises withdrawing enzymes corresponding to at least one of the enzyme inhibitors in the sample by means of chromatography and analysing the present concentration and/or activity of the specific inhibitors by means of specific assays.

24. A process according to claim 23 characterized in that the sample is passed through a column (1) filled with a chromatographic carrier, that is treated with a substance capable of binding enzymes.

25. A process according to claim 23 or 24 characterized in that the manipulated sample is diluted with a suitable column buffer in a definite manner.

26. A process according to one of the claims 23 to 25 characterized in that there is added an appropriate measuring buffer to the manipulated sample as to establish definite experimental conditions.

27. A process according to one of the claims 23 to 26 characterized in that the material involved in the assay for measuring the concentration and/or activity of the inhibitor is thermostated at least during the incubation time.

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